422 Rec'd PCT/PTO 16 AUG 2000

FORM PTO-1390 (REV 5-93)	U S DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	ATTORNEY'S DOCKET NO
	TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371	4512/00004
		U.S. APPLICATION NO (if known, See 37 CFR 1.5) 09/622433
INTERNATIONAL APPLICATION NO. PCT/GB99/00511	INTERNATIONAL FILING DATE 18 February 1999 (18.02.99)	PRIORITY DATE CLAIMED 18 February 1998 (18.02.98)

TITLE OF INVENTION
PHARMACEUTICAL FORMULATION OF A DIDEMNIN COMPOUND

APPLICANT(S) FOR DO/EO/US
NUYEN, Bastiaan; BEIJNEN, Jacob Hendrik;; HENRAR, Roland Elizabeth Cornelis; GOMEZ, Andres; JIMENO, José

Applicant herewith submits to the United State Designated/Elected Office (DO/EO/US) the following items and other information:

1. ■ This is a FIRST submission of items concerning a filing under 35 U.S.C. 371.
2. ☐ This is a SECOND or SUBSEQUENT submission of items concerning a filing under 35 U.S.C. 371.
3. ■ This express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1).
4. ■ A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.
5. ■ A copy of the International Application as filed (35 U.S.C. 371(c)(2))
   a. ■ is transmitted herewith (required only if not transmitted by the International Bureau).
   b. ■ has been transmitted by the International Bureau.
   c. ☐ is not required, as the application was filed in the United States Receiving Office (RO/US).
6. ☐ A translation of the International Application into English (35 U.S.C. 371(c)(2)).
7. ■ Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3))
   a. ☐ are transmitted herewith (required only if not transmitted by the International Bureau).
   b. ☐ have been transmitted by the International Bureau.
   c. ☐ have not been made; however, the time limit for making such amendments has NOT expired.
   d. ■ have not been made and will not be made.
8. ☐ A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).
9. ☐ An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).
10. ☐ A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).

Items 11-16 below concern other document(s) or information included:

11. ☐ An Information Disclosure Statement under 37 C.F.R. 1.97 and 1.98.
12. ☐ An Assignment document for recording. A separate cover sheet in compliance with 37 C.F.R. 3.28 and 3.31 is included.
13. ☐ A FIRST preliminary amendment.
    ☐ A SECOND or SUBSEQUENT preliminary amendment.
14. ☐ A substitute specification.
15. ☐ A change of power of attorney and/or address letter.
16. ☐ Other items or information:

International Search Report (translated) (EPO)

U.S. APPLICATION NO (If known, See 37 CFR 1.5) 09/622433	INTERNATIONAL APPLICATION NO. PCT/GB99/00511	ATTORNEY'S DOCKET NO. 4512.00004

17. The following fees are submitted:	CALCULATIONS	PTO USE ONLY
Basic National Fee (37 CFR 1.492(a)(1)-(5):		
Search Report has been prepared by the EPO or JPO $840.00		
International preliminary examination fee paid to USPTO (37 CFR 1.482) $670.00		
No International preliminary examination fee paid to USPTO (37 CFR 1.482), but international search fee paid to USPTO (37 CFR 1.445(a)(2)) $700.00		
Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO $970.00		
International preliminary examination fee paid to USPTO (37 CFR 1.482) and all claims satisfied provisions of PCT Article 33(1)-(4) $ 96.00		
ENTER APPROPRIATE BASIC FEE AMOUNT =	$ 840.00	
Surcharge of $130.00 for furnishing the oath or declaration later than 20 or 30 months from the earliest claimed priority date (37 CFR 1.492(e).	$ -0-	

CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE		
Total Claims	11 - 20 =	-0-	X $ 18.00	$	
Independent Claims	3 - 3 =	-0-	X $ 78.00	$	
Multiple dependent claims (if applicable)			X $260.00	$	
TOTAL OF ABOVE CALCULATIONS =				$ 840.00	
Reduction by 1/2 for filing by small entity, if applicable. Verified Small Entity statement must also be filed (note 37 CFR 1.9, 1.27, 1.28).				$ -0-	
SUBTOTAL =				$ 840.00	
Processing fee of $130.00 for furnishing the English translation later than 20 or 30 months from the earliest claimed priority date (37 CFR 1.492(f).				$ -0-	
TOTAL NATIONAL FEE =				$ 840.00	
Fee for recording the enclosed assignment (37 CFR 1.21(h). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). $40.00 per property.				$ -0-	
TOTAL FEES ENCLOSED =				$ -0-	
				Amount to be: refunded	$
				charged	$840.00

a. ☐ A check in the amount of $_____ to cover the above fees is enclosed.

b. ■ Please charge my Deposit Account No. 19-0733 in the amount of $840.00 to cover the above fees.

c. ■ The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 19-0733. A duplicate copy of this sheet is enclosed.

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO:

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Telephone: (617) 227-7111

August 16, 2000

SIGNATURE
Ernest V. Linek
Registration No. 29,822

PTO/SB/64 (10-01)
Approved for use through 10/31/2002. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

PETITION FOR REVIVAL OF AN APPLICATION FOR PATENT ABANDONED UNINTENTIONALLY UNDER 37 CFR 1.137(b)	Docket Number (Optional) 4512/00004

First named inventor: **Nuyen et al.**

Application No.: **09/622,433** Art Unit: **Unassigned**

Filed: **16 August 2000** Examiner:

Title: **Pharmaceutical Formulation of a Didemnin Compound**

Attention: Office of Petitions
Assistant Commissioner for Patents
Box DAC
Washington, D.C. 20231

NOTE: If information or assistance is needed in completing this form, please contact Petitions Information at (703) 305-9282.

The above-identified application became abandoned for failure to file a timely and proper reply to a notice or action by the United States Patent and Trademark Office. The date of abandonment is the day after the expiration date of the period set for reply in the Office notice or action plus an extensions of time actually obtained.

APPLICANT HEREBY PETITIONS FOR REVIVAL OF THIS APPLICATION

NOTE: A grantable petition requires the following items:
(1) Petition fee;
(2) Reply and/or issue fee;
(3) Terminal disclaimer with disclaimer fee – required for all utility and plant applications filed before June 8, 1995; and for all design applications; and
(4) Statement that the entire delay was unintentional.

1. Petition fee

☐ Small entity-fee $_____ (37 CFR 1.17(m)). Applicant claims small entity status. See 37 CFR 1.27.

☒ Other than small entity - fee $ 1240.00 (37 CFR 1.17(m))

2. Reply and/or fee

A. The reply and/or fee to the above-noted Office action in the form of Missing 4th Inventor Signature on Dec/POA (identify type of reply):
☐ has been filed previously on _____.
☒ is enclosed herewith.

B. The issue fee of $_____.
☐ has been paid previously on _____.
☐ is enclosed herewith.

05/21/2002 LLANDGRA 00000088 190733 09622433
01 FC:141 1280.00 CH

Burden Hour Statement: This form is estimated to take 1.0 hour to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.

PTO/SB/64 (10-01)
Approved for use 10/31/2002. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

3. Terminal disclaimer with disclaimer fee

XX Since this utility/plant application was filed on or after June 8, 1995, no terminal disclaimer is required.

☐ A terminal disclaimer (and disclaimer fee (37 CFR 1.20(d)) of $ _____ for a small entity or $ _____ for other than a small entity) disclaiming the required period of time is enclosed herewith (see PTO/SB/63).

4. STATEMENT: The entire delay in filing the required reply from the due date for the required reply until the filing of a grantable petition under 37 CFR 1.137(b) was unintentional. [NOTE. The United States Patent and Trademark Office may require additional information if there is a question as to whether either the abandonment or the delay in filing a petition under 37 CFR 1.137(b) was unintentional (MPEP 711.03(c), subsections (III)(C) and (D))].

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

10 May 2002
Date

[Signature]
Signature

Telephone Number: (617) 227-7111

Ernest V. Linek (Reg. No. 29,822)
Typed or printed name

Banner & Witcoff, Ltd.
28 State Street, 28th Floor
Address
Boston, MA 02109-1775

Enclosures: XX Fee Payment

XX Reply

Please chareg all fees to Deposit Account No. 19-0733.

☐ Terminal Disclaimer Form

☐ Additional sheets containing statements establishing unintentional delay

☐ Other: ________________

CERTIFICATE OF MAILING OR TRANSMISSION [37 CFR 1.8(a)]

I hereby certify that this correspondence is being:

☐ deposited with the United States Postal Service on the date shown below with sufficient postage as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Box DAC, Washington, D.C. 20231.

XX transmitted by facsimile on the date shown below to the United States Patent and Trademark Office at (703) 308-6916.

10 May 2002
Date

[Signature]
Signature

Ernest V. Linek
Type or printed name of person signing certificate

PHARMACEUTICAL FORMULATION OF A DIDEMNIN COMPOUND

The present invention relates to a pharmaceutical formulation, and more particularly a pharmaceutical formulation of a didemnin compound.

THE BACKGROUND

US Patent 5,294,603 to Rinehart claims a pharmaceutical composition comprising a didemnin, in combination with a pharmaceutically acceptable carrier, excipient or diluent. In that patent, extensive results are given for testing for biological activity, notably assay results for cytotoxicity and antiviral activity.

THE PROBLEM

In practice, there are some difficulties in preparing pharmaceutical compositions of didemnin compounds suited for administration to patients, and there is especially a need for a stable parental pharmaceutical dosage form. More specifically, didemnin compounds such as dehydrodidemnin B, also known as aplidine, require mixing with bulking agents, such as mannitol, for optimal,

stable preparation of pharmaceutical dosage forms, in particular lyophilised preparations,

Certain bulking agents for this purpose, such as mannitol, require water for solubilisation, while drugs such as aplidine are poorly soluble in water. However, drug delivery to patients requires resuspending of the lyophilised materials before use.

THE INVENTION

The present invention solves the problem by providing a pharmaceutical composition of a didemnin compound, comprising firstly a lyophilised didemnin preparation including water-soluble materials and secondly a reconstitution solution of mixed solvents. The mixed solvents comprise an aqueous solvent, with the water serving to dissolve the water soluble material and the other solvent serving to dissolve the didemnin compound.

PREFERRED EMBODIMENTS

The pharmaceutical formulation of this invention is typically a stable parental pharmaceutical dosage form suited for reconstitution for administration to patients as an antitumor treatment. The invention solves the problem for drugs such as aplidine, which must be presented as lyophilised mixtures of two or more substances soluble in incompatible solvents. It preferably

provides, separately bottled or otherwise contained, a premixed three component surfactant/alkanol/water mixture of solvents. In order to allow for proper resuspension of such pharmaceutical dosage forms, the separately packaged solvent mixture is provided to be added to the dry lyophilised preparations containing the drug and water soluble substances such as mannitol, before administration for treatment of disease.

Preferred didemnin compounds for the pharmaceutical compositions of this invention include didemnins and didemnin derivatives, such as dehydrodidemnins, nordidemnins, didemnin congeners and didemnin analogs. The present invention is particularly directed at didemnins with limited water solubility, including for example dehydrodidemnin B, also known as aplidine.

The antitumour agent aplidine (dehydrodidemnin B) is a natural occurring cyclic depsipeptide isolated from the Mediterranean runicate *Aplidium albicans*. Aplidine has been characterised by using several chromatographic and spectrometric techniques. Solubility testing showed that aplidine exhibits poor aqueous solubility. Moreover, the long-term stability of aplidine in solution is currently unknown.

The lyophilised didemnin preparation is preferably prepared by freeze drying a didemnin/alkanol/water mix, especially using t-butanol as the alkanol. The alkanol/water mix suitably contains 25 to 60% v/v alkanol. A bulking agent such as mannitol can

also be included, though other conventional water-soluble additives may be included, known to be of utility in the preparation of such lyophilised dosage forms.

The reconstitution solution preferably comprises a surfactant/alkanol/water mix, especially using a nonionic surfactant and ethanol as the alkanol. The surfactant is suitably 10 to 25% v/v of the mix; the alkanol is suitably 10 to 25% v/v of the mix; and the water is suitably 50 to 80% v/v of the mix.

EXAMPLES

Freeze-drying was performed from a 1.0 mg/ml solution aplidine in 40% v/v t-butanol in water for injection ("WFI) containing 25 mg/ml mannitol as bulking agent. Differential scanning calorimetry studies were conducted to determine the freeze-drying cycle parameters. The prototype, containing 1.0 mg aplidine and 25 mg mannitol per vial was found to be the optimal formulation in terms of solubility, length of the freeze-during cycle and dosage requirements.

A solution composed of 15/15/70% (v/v/v) Cremophor EL/ethanol absolute/WFI was found to the optimal reconstitution solution, Cremophor EL being a glycerol-polyethylene glycol ricinoleate available from BASF in Germany.

Dilutions of reconstituted product with normal saline up to 1:200 showed it to be stable for at least 24 hours after preparation. Quality control of the freeze-dried formulation demonstrated that the manufacturing process does not change the integrity of aplidine. Shelf-life data, available thus far, show that the formulation is stable for at least 6 months when stored at +4°C in the dark.

Thus, the preferred aplidine product of this invention is a dual-package containing:

an injection vial containing aplidine 1 mg/vial lyophilized product, and an injection vial containing 2 ml of 15/15/70% (v/v/v) Cremophor EL/ethanol/water as reconstruction solution.

The use of 15/15/70% (v/v/v) Cremophor EL/ethanol/water as reconstitution solution for a lyophilized product is unprecedented. Thus far, the combination of Cremophor EL/ethanol in commercial available products has been used exclusively as solution vehicle (e.g., taxol or cyclosporine).

The development of the Cremophor EL/ethanol/water vehicle provides a potent co-solvent/surfactant system which can be applied as reconstitution solution in future drug formulations and allows the addition of a water soluble bulking agent such as mannitol. Furthermore, by decreasing the relative amount of Cremophor EL, a less toxic vehicle is created.

The manufacturing procedure of the lyophilized product has also a special feature. Normally, freeze-drying of a drug is performed from a drug solution in water. In the case of aplidine, a 40% (v/v) t-butanol/water mixture is preferably used as freeze-drying medium. Although previously described (e.g. rhizoxin), freeze-drying from a 40% t-butanol/water mixture is not common practice.

In conclusion, the combination of lyophilisation of a drug from a t-butanol/water mixture and the subsequent reconstitution of the lyophilized product with 15/15/70% (v/v/v) Cremophor EL/ethanol/water is unique.

CLAIMS:

1. A pharmaceutical composition of a didemnin compound, comprising firstly a lyophilised didemnin preparation including water-soluble material and secondly a reconstitution solution of mixed solvents.

2. A didemnin composition according to claim 1, intended for reconstitution for administration to patients as an antitumor treatment.

3. A didemnin composition according to claim 1 or 2, wherein the didemnin is chosen from didemnins, dehydrodidemnins, nordidemnins, didemnin congeners and didemnin analogs.

4. A didemnin composition according to claim 3, wherein the didemnin compound is aplidine.

5. A didemnin composition according to any preceding claim, wherein the reconstitution solution comprises an alkanol/water mix.

6. A didemnin composition according to claim 5, wherein the reconstitution solution includes a nonionic surfactant.

7. A didemnin composition according to claim 6, wherein the nonionic surfactant is 10 to 25% v/v of the solution; the

alkanol is ethanol and is 10 to 25% v/v of the solution; and the water is 50 to 80% v/v of the solution.

8. A didemnin composition according to any preceding claim, which comprises a vial of lyophilised didemnin preparation including a water-soluble bulking agent, and a separate vial of a premix of non-ionic surfactant/ethanol/water.

9. A method of preparing a pharmaceutical composition of a didemnin compound, which comprises freeze drying a didemnin/water-soluble additive/alkanol/water mix to provide a lyophilised first component, and separately providing an alkanol/water mix as reconstitution solution.

10. A method according to claim 9 wherein the alkanol in the mix is t-butanol.

11. A method according to claim 9 or 10 wherein the amount of alkanol in the alkanol/water mix is 25 to 60% v/v.

PCT

WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

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9803448.1 18 February 1998 (18.02.98) GB

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(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published

With international search report.

Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(54) Title: PHARMACEUTICAL FORMULATION OF A DIDEMNIN COMPOUND

(57) Abstract

A stable pharmaceutical composition of a didemnin compound, comprises firstly a lyophilised didemnin preparation including water–soluble material and secondly a reconstitution solution of mixed solvents.

Document [redacted]795

Attorneys' Docket No. 4512/00004

USA

DECLARATION AND POWER OF ATTORNEY FOR PATENT APPLICATION

As below-named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled: Pharmaceutical Formulation of a Didemnin Compound

which is described and claimed in:

[ ] the attached specification
[ ] the specification in application Serial No. **09/622,433** filed **16 August 2000, and**
[x] PCT International Application No. PCT/GB99/00511 filed Feb 18, 1999
(if applicable) and amended on _____ under Article 19 PCT
and on _____ under Article 34 PCT

I hereby state that I have reviewed and understand the contents of the above-identified application specification, including the claims, as amended by any amendment specifically referred to herein.

I acknowledge the duty to disclose all information known to me that is material to patentability in accordance with Title 37, Code of Federal Regulations, §1.56.

I hereby claim foreign priority benefits under Title 35, United States Code §119 of any foreign applications(s) for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate having a filing date before that of the application on which priority is claimed:

Number	Country	Date Filed	Priority Claimed
9803448.1	United Kingdom	Feb 18, 1998	[x]yes [ ]no
			[ ]yes [ ]no
			[ ]yes [ ]no
			[ ]yes [ ]no

I hereby claim the benefit under Title 35, United States Code §1.20, of the United States Application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of Title 35, United States Code, §112, I acknowledge the duty to disclose all information that is material to patentability in accordance with Title 37, Code of Federal Regulations, §1.56, and which became available to me between the filing date of the prior application and the national or PCT international filing date of this application:

Application Serial No.	Filing Date	Status (patented, pending, abandoned)

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and believed to be true; and further that these statements were made with the knowledge that wilful false statements and the like so made are punishable by fine or imprisonment or both under Section 1001 of Title 18 of the United States Code and that such wilful false statements may jeopardize the validity of the application or any patent issued thereon.

Documen[illegible]7837

I hereby appoint

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BODNER, Jordan	42,338	KATZ, Robert S.	36,402	PRATT, Thomas K.	37,210
BUROW, Scott A.	42,373	KLEIN, William J.	43,719	RENK, Christopher J.	33,761
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HANLON, Brian E	40,449	MITRIUS, Janice V.	43,808	WOLFFE, Susan A.	33,568
HART, Robert P.	35,184	MORENO, Christopher P.	38,566	WRIGHT, Bradley C	38,061
HEMMENDINGER, Lisa M	42,653	NELSON, Jon O.	24,566		
HILLMAN, Lisa	43,673	NIEGOWSKI, James A.	28,331		

jointly, and each of them severally, my attorneys and attorney, with full power of substitution, delegation and revocation, to prosecute this application, to make alterations and amendments therein, to receive the patent and to transact all business in the Patent and Trademark Office connected therewith. Please direct all correspondence and telephone calls to:

Ernest V. Linek
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1-00

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2-00

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Post Office Address:	The Netherland Cancer Institute/Slotervaart Hospital Dept., of Pharmacology EC Amsterdam, 1066, Netherlands NLX

3-00

Full Name of third Inventor:	~~Henrar, Roland Elizabeth Cornelis~~
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5-00

Full Name of fifth Inventor:	Jimeno, José
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Citizenship:	Spanish
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Full Name of sixth Inventor: ______
Residence: ______
Citizenship: ______
Post Office Address: ______

Signature of first inventor: ______ Date: 25/1/1

Signature of second inventor: ______ Date: 26/01/2001

Signature of third inventor: ______ Date: 12/2/2001

Signature of fourth inventor: ______ Date: ______

Signature of fifth inventor: ______ Date: 22/01/01

Signature of sixth inventor: ______ Date: ______

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Document #: 597795

Attorneys' Docket No.

USA

DECLARATION AND POWER OF ATTORNEY FOR PATENT APPLICATION

As below-named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled: Pharmaceutical Formulation of a Didemnin Compound

which is described and claimed in:

[ ] the attached specification

[ ] the specification in application Serial No. _____ filed _____

[x] PCT International Application No. PCT/GB99/00511 filed Feb 18, 1999

(if applicable) and amended on _____ under Article 19 PCT

and on _____ under Article 34 PCT

I hereby state that I have reviewed and understand the contents of the above-identified application specification, including the claims, as amended by any amendment specifically referred to herein.

I acknowledge the duty to disclose all information known to me that is material to patentability in accordance with Title 37, Code of Federal Regulations, §1.56.

I hereby claim foreign priority benefits under Title 35, United States Code §119 of any foreign applications(s) for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate having a filing date before that of the application on which priority is claimed:

Number	Country	Date Filed	Priority Claimed
9803448.1	United Kingdom	Feb 18 1998	[x]yes [ ]no
			[ ]yes [ ]no
			[ ]yes [ ]no
			[ ]yes [ ]no

I hereby claim the benefit under Title 35, United States Code §120, of the United States Application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of Title 35, United States Code, §112, I acknowledge the duty to disclose all information that is material to patentability in accordance with Title 37, Code of Federal Regulations, §1.56, and which became available to me between the filing date of the prior application and the national or PCT international filing date of this application:

Application Serial No.	Filing Date	Status (patented, pending, abandoned)

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and believed to be true; and further that these statements were made with the knowledge that wilful false statements and the like so made are punishable by fine or imprisonment or both under Section 1001 of Title 18 of the United States Code and that such wilful false statements may jeopardize the validity of the application or any patent issued thereon.

Document #: 597837

"by appoint

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BANNER, Donald W.	17,097	HOSCHEIT, Dale H.	19,090	PATHAK, Ajay S.	38,266
BANNER, Mark T	29,888	IWANICKI, John P.	34,628	PAYNE, Stephen S.	35,316
BANNER, Pamela J.	33,644	JACKSON, Thomas H.	29,808	PETERSON, Thomas L.	30,969
BECKETT, William W.	18,262	KAGAN, Sarah A.	32,141	POTENZA, Joseph M.	28,175
BODNER, Jordan	42,338	KATZ, Robert S.	36,402	PRATT, Thomas K.	37,210
BUROW, Scott A.	42,373	KLEIN, William J.	43,719	RENK, Christopher J.	33,761
CALLAHAN, James V.	20,095	KRAUSE, Joseph P.	32,578	RESIS, Robert H.	32,168
CHANG, Steve S	42,402	LINEK, Ernest V.	29,822	RIVARD, Paul M.	43,446
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COOPERMAN, Marc S.	34,143	MALONE, Dale A.	32,155	SHIPLEY, Charles W	28,042
CURTIN, Joseph P	34,571	MANNAVA, Ashok K.	P45,301	SKERPON, Joseph M.	29,864
DAWSON, John R.	39,504	McDERMOTT, Peter D.	29,411	SPAR, Elizabeth	45,123
DEMOOR, Laura J.	39,654	McKEE, Christopher L.	32,384	STOCKLEY, D. J.	34,257
EVANS, Thomas L.	35,805	McKIE, Edward F.	17,335	VAN ES, J Pieter	37,746
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FISHER, Daniel E.	34,162	MEECE, Timothy C.	38,555	WITCOFF, Sheldon W.	17,399
FISHER, William J.	32,133	MEEKER, Frederic M.	35,282	WOLFF, Kevin A.	42,233
GLEMBOCKI, Christopher R.	38,800	MILLER, Charles L.	43,805	WOLFFE, Franklin D.	19,724
HANLON, Brian E.	40,449	MITRIUS, Janice V.	45,808	WOLFFE, Susan A.	33,568
HART, Robert P.	35,184	MORENO, Christopher P.	38,566	WRIGHT, Bradley C.	38,061
HEMMENDINGER, Lisa M.	42,653	NELSON, Jon O.	24,566		
HILLMAN, Lisa	43,673	NIEGOWSKI, James A.	28,331		

jointly, and each of them severally, my attorneys and attorney, with full power of substitution, delegation and revocation, to prosecute this application, to make alterations and amendments therein, to receive the patent and to transact all business in the Patent and Trademark Office connected therewith. Please direct all correspondence and telephone calls to:

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Full Name of sixth Inventor: ______________________
Residence: ______________________
Citizenship: ______________________
Post Office Address: ______________________
____

Signature of first inventor:		Date:	
Signature of second inventor:		Date:	
Signature of third inventor:		Date:	
Signature of fourth inventor:	X [signature]	Date:	23/Abril/2002
Signature of fifth inventor:		Date:	
Signature of sixth inventor:		Date:	